```
FILE 'USPAT' ENTERED AT 08:45:23 ON 26 MAY 94

  * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * *
  *                W E L C O M E   T O   T H E                    *
  *          U. S.   P A T E N T   T E X T   F I L E              *
  * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * *

=> e jutila/in
E1            1     JUTERBOCK, KARSTEN/IN
E2            1     JUTIER, PIERRE/IN
E3            0 --> JUTILA/IN
E4            1     JUTILA, PENTTI K/IN
E5            1     JUTILA, RAYMOND E/IN
E6            2     JUTILA, RAYMOND EINO/IN
E7            1     JUTKEVICH, VALERY I/IN
E8            1     JUTKEVICH, VALERY IVANOVICH/IN
E9            1     JUTO, YASURO/IN
E10           1     JUTRAS, GILLES/IN
E11           1     JUTRAS, MARIO/IN
E12           1     JUTRAS, MARTIAL/IN

=> s lam(w)1 or lecam(w)1 or l(w)selectin
           605 LAM
       1802011 1
                                          11 LAM(W)1
             6 LECAM
       1802011 1
                           1 LECAM(W)1
        396493 L
            24 SELECTIN
             1 L(W)SELECTIN
L1          11 LAM(W)1 OR LECAM(W)1 OR L(W)SELECTIN

=> s elam or elam(w)1 or e(w)selectin
                                                85 ELAM
            85 ELAM
       1802011 1
            18 ELAM(W)1
       1034832 E
            24 SELECTIN
             2 E(W)SELECTIN
L2          85 ELAM OR ELAM(W)1 OR E(W)SELECTIN

=> s l1 and l2
L3           5 L1 AND L2

=> d l3 1-5

1.   5,304,640, Apr. 19, 1994, DNA sequence encoding a selectin
ligand;
Laurence A. Lasky, et al., 536/23.5; 435/69.1, 172.3, 240.2, 320.1
[IMAGE
AVAILABLE]
```

2. 5,252,602, Oct. 12, 1993, Effects of misoprostol on allergic responses; Rafeul Alam, et al., 514/530, 573, 826 [IMAGE AVAILABLE]

3. 5,227,369, Jul. 13, 1993, Compositions and methods for inhibiting leukocyte adhesion to CNS myelin; Steven Rosen, et al., 514/23, 2, 3, 4, 8, 885, 903 [IMAGE AVAILABLE]

4. 5,198,424, Mar. 30, 1993, Functionally active selectin-derived peptides; Rodger P. McEver, 514/13; 424/1.37, 1.69; 427/2; 514/12, 14, 15, 16; 530/324, 325, 326, 327; 623/11 [IMAGE AVAILABLE]

5. 5,151,360, Sep. 29, 1992, Effect of N,N,N-trimethylsphingosine on protein kinase-C activity, melanoma cell growth in vitro, metastatic potential in vivo and human platelet aggregation; Kazuko Handa, et al., 435/240.2, 240.1 [IMAGE AVAILABLE]

```
=> s l3 and common(w)epitope
        472958 COMMON
          1273 EPITOPE
            62 COMMON(W)EPITOPE
L4           0 L3 AND COMMON(W)EPITOPE

=> s l3 and scr
         10597 SCR
L5           1 L3 AND SCR

=> d l5 1
```

1. 5,304,640, Apr. 19, 1994, DNA sequence encoding a selectin ligand; Laurence A. Lasky, et al., 536/23.5; 435/69.1, 172.3, 240.2, 320.1 [IMAGE AVAILABLE]

=>

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  * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * *
  *                  W E L C O M E   T O   T H E                  *
  *          U. S.   P A T E N T   T E X T   F I L E              *
  * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * *

=> e jutila/in
E1            1     JUTERBOCK, KARSTEN/IN
E2            1     JUTIER, PIERRE/IN
E3            0 --> JUTILA/IN
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E5            1     JUTILA, RAYMOND E/IN
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E7            1     JUTKEVICH, VALERY I/IN
E8            1     JUTKEVICH, VALERY IVANOVICH/IN
E9            1     JUTO, YASURO/IN
E10           1     JUTRAS, GILLES/IN
E11           1     JUTRAS, MARIO/IN
E12           1     JUTRAS, MARTIAL/IN

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           605 LAM
       1802011 1
                                          11 LAM(W)1
             6 LECAM
       1802011 1
                           1 LECAM(W)1
        396493 L
            24 SELECTIN
             1 L(W)SELECTIN
L1          11 LAM(W)1 OR LECAM(W)1 OR L(W)SELECTIN

=> s elam or elam(w)1 or e(w)selectin
                                                85 ELAM
            85 ELAM
       1802011 1
            18 ELAM(W)1
       1034832 E
            24 SELECTIN
             2 E(W)SELECTIN
L2          85 ELAM OR ELAM(W)1 OR E(W)SELECTIN

=> s l1 and l2
L3           5 L1 AND L2

=> d l3 1-5

1.   5,304,640, Apr. 19, 1994, DNA sequence encoding a selectin
ligand;
Laurence A. Lasky, et al., 536/23.5; 435/69.1, 172.3, 240.2, 320.1
[IMAGE
AVAILABLE]
```

2. 5,252,602, Oct. 12, 1993, Effects of misoprostol on allergic responses; Rafeul Alam, et al., 514/530, 573, 826 [IMAGE AVAILABLE]

3. 5,227,369, Jul. 13, 1993, Compositions and methods for inhibiting leukocyte adhesion to CNS myelin; Steven Rosen, et al., 514/23, 2, 3, 4, 8, 885, 903 [IMAGE AVAILABLE]

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5. 5,151,360, Sep. 29, 1992, Effect of N,N,N-trimethylsphingosine on protein kinase-C activity, melanoma cell growth in vitro, metastatic potential in vivo and human platelet aggregation; Kazuko Handa, et al., 435/240.2, 240.1 [IMAGE AVAILABLE]

```
=> s l3 and common(w)epitope
        472958 COMMON
          1273 EPITOPE
            62 COMMON(W)EPITOPE
L4           0 L3 AND COMMON(W)EPITOPE

=> s l3 and scr
         10597 SCR
L5           1 L3 AND SCR

=> d l5 1
```

1. 5,304,640, Apr. 19, 1994, DNA sequence encoding a selectin ligand; Laurence A. Lasky, et al., 536/23.5; 435/69.1, 172.3, 240.2, 320.1 [IMAGE AVAILABLE]

=>

```
          19863  EL
           4345  246
     S1       4  EL(W)246
?^Q
...completed examining records
     S2       2  RD S1 (unique items)
?^Q

 2/7/1     (Item 1 from file: 55)
DIALOG(R)File  55:BIOSIS PREVIEWS(R)
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9535279     BIOSIS Number: 94040279
  CHARACTERIZATION OF A FUNCTIONALLY IMPORTANT AND EVOLUTIONARILY
WELL-CONSERVED EPITOPE MAPPED TO THE SHORT CONSENSUS REPEATS OF E
SELECTIN
AND L SELECTIN
  JUTILA M A; WATTS G; WALCHECK B; KANSAS G S
  VETERINARY MOLECUALR BIOLOGY, MONTANA STATE UNIVERSITY, BOZEMAN,
MT
59717.
  J EXP MED 175 (6). 1992.  1565-1573.   CODEN: JEMEA
  Full Journal Title:  Journal of Experimental Medicine
  Language: ENGLISH
  Selectins reperesent a new family of adhesion molecules,
expressed by
leukocytes and endothelial cells, that are involved in the
regulation of
leukocyte traffic. Here we have characterized a new monoclonal
antibody
(mAb) (EL-246) that recognizes both human leukocyte L-selectin
(previously
called LAM-1, LECAM-1, or gp90MEL-14) and endothelial cell
E-selectin
(previously called ELAM-1). EL-246 recognized a 110-kD protein
expressed on
cells transfected with E-selectin cDNA and stained many
postcapillary
venules in inflamed human tonsil. EL-246 also stained human
peripheral
blood leukocytes and showed identity with anti-L-selectin mAb in
two-color
flow cytometric analysis. The expression of the leukocyte EL-246
antigen
was regulated in the same manner as L-selectin and EL-246
recognized
anti-L-selectin mAb affinity-purified antigen in SDA/PAGE
Western blot
analysis. Further, L-selectin cDNA transfectants were specifically
stained
by EL-246. EL-246 blocked >95% of lymphocyte adhesion to
peripheral lymph
node high endothelial venules and >90% of neutrophil adhesion to
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E-selectin transfectants. In addition to the EL-246 epitope being expressed on two different human selectins, it was detected on L-selectin from a variety of different animals. Interestingly domain mapping studies localized the EL-246 epitope to the short consensus repeat (SCR) domains of L-selectin. EL-246 is the first mAb that recognizes two different selectins and potentially defines a functional epitope encoded by the SCR domains. Inhibitors of selectin function targeted to this region would be expected to have the added advantage of simultaneously blocking the activity of two distinct of adhesion protein involved in inflammation.

2/7/2 (Item 1 from file: 72)
DIALOG(R)File 72:EMBASE

9171016 EMBASE No: 94118088
Survival in lung reperfusion injury is improved by an antibody that binds and inhibits L- and E-selectin
Steinberg J.B.; Mao H.-Z.; Niles S.D.; Jutila M.A.; Kapelanski D.P.
Division of Cardiothoracic Surgery, UCSD Medical Center, 225 Dickinson St., San Diego, CA 92103-8892 USA
J. HEART LUNG TRANSPLANT. (USA) , 1994, 13/2 (306-318) CODEN: JHLTE
ISSN: 1053-2498
LANGUAGES: English SUMMARY LANGUAGES: English
The selectins are a three-member family of leukocyte, platelet, and endothelial cell adhesion proteins that mediate leukocyte traffic into normal and inflamed tissues. P-selectin is expressed by endothelial cells and platelets, E-selectin by endothelial cells, and L-selectin by circulating leukocytes. To determine if selectin-mediated leukocyte adhesion influences the development of lung reperfusion injury, we studied hemodynamics and respiratory and inert gas exchange in sheep subjected to 3-hour in situ left lung ischemia followed by 6-hour left lung reperfusion with the right lung excluded. Ten minutes before reperfusion, eight

animals
received EL-246 (1 mg/kg intravenously), a novel antihuman selectin
antibody that recognizes and blocks both L- and E-selectin and cross-reacts
in sheep. Eight control animals with ischemia received no treatment,
whereas three received an isotype-matched antihuman L-selectin antibody
that does not cross-react in sheep (DREG-56, 1 mg/kg intravenously). Eight
sham control sheep underwent an identical operative procedure but were
never subjected to ischemia. Volume- cycled, pressure-limited (20 cm H2O)
mechanical ventilation was consistent in all animals throughout the
experiment. Six-hour survival in EL-246 recipients (100%) was significantly
higher than in either ischemic control sheep (37.5%) or DREG-56 recipients
(33.3%), but gravimetric lung water was equivalent in EL-246 recipients
(5.9 plus or minus 1.7 ml/kg), ischemic control sheep (8.3 plus or minus
3.0 ml/kg), and DREG-56 recipients (9.1 plus or minus 2.6 ml/kg). Although
inert gas shunt at one-half hour of reperfusion was no different when
contrasted in EL- 246 recipients (15% plus or minus 8%), ischemic control
sheep (30% plus or minus 25%), and DREG-56 recipients (35% plus or minus
21%), shunts in EL-246 recipients resolved (4% plus or minus 4%) within the
6-hour study period and were associated with a concomitant improvement in
respiratory gas exchange. Peripheral blood neutrophil counts increased
after both EL-246 and DREG-56 administration, suggesting that the
beneficial effect of EL-246 was not incurred by leukocyte depletion. We
conclude that mechanisms other than activated neutrophils may account for
the initial deterioration of respiratory gas exchange in lung reperfusion
injury and inhibition of selectin function improves survival by preventing
leukocyte-mediated amplification of this early process.
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